



**REMARKS**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

**I. The Amendments to the Claims**

Claims 10 and 20-22 are amended. Claim 10, as amended, specifies that a plurality of hollow pins are connected to a drive that introduces a distal end of the hollow pins into the sample container *offset from an animal cell* colony, and the animal cell colonies are picked from the medium by the hollow pins *at an offset distance*. Support for the amendment to claim 10 can be found, *inter alia*, in the specification at page 12, lines 20-30, and at page 17, lines 16-17. The amendment to claims 20-22 incorporates step (e) of claim 1. Support for the amendment to claims 20-22 can be found, *inter alia*, in claim 1, as previously presented.

New claims 23-32 are added. These claims specify the range of the offset distance at which the animal cell colonies are picked by the hollow pins. Support for new claims 23-32 can be found, *inter alia*, in Figure 7 and page 12, lines 18-30, of the specification. This section in the specification describes an inner pin (item 64 in Figure 7), which is recessed inside the outer pin (item 62 in Figure 7) by a distance d1. The outer pin is recessed from the bottom of the sample container by a distance d2. Thus, the offset distance claimed in the present application is the sum of d1 and d2. The specification at page 12, lines 18-30, defines d1 as having values of 0.1 to 2.0 mm, and d2 as having values of 0.0 to 2.0 mm. Thus, the range of d1 + d2 is 0.1 to 4.0 mm.

Upon entry of the foregoing amendments, claims 1-32 will be pending in the application, with claims 1 and 10 being the independent claims. These amendments do not introduce new matter into the application. Applicants respectfully urge the entry of these amendments after final because they will not require a new search and are believed to place the application in condition for allowance, or at least in better condition for appeal.

## **II. The Interview with the Examiner**

Applicants thank Examiner Nathan Andrew Bowers for the courtesy extended in the personal interview held on October 12, 2006 with Applicants' representative. The claims presented herein and the following remarks reflect the issues that were discussed in the interview.

## **III. The Rejections Under 35 U.S.C. § 103(a)**

### **A. Rejection over Uber in view of Bienert**

The Office Action, at pages 2-3, maintains the rejection of claims 10 and 21 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Uber *et al.*, *Biotechniques*, 11(5): 642-646 (1991 ("Uber")) in view of U.S. Patent Application Publication No. 20010019845 ("Bienert"). Applicants respectfully traverse the rejection.

The Patent Office bears the initial burden of factually supporting any *prima facie* conclusion of obviousness under 35 U.S.C. § 103. The MPEP § 2142 sets forth the criteria necessary to satisfy this burden:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As discussed below, there is no *prima facie* case of obviousness, because none of these three criteria is satisfied.

## **1. Summary of the Claimed Invention**

The presently claimed invention is directed to a method for automated picking of animal cell colonies. The method employs a picking head comprising a plurality of hollow pins to pick the colonies. The method comprises introducing a distal end of a hollow pin into the medium proximate to the animal cell colony *by an offset distance* and aspirating the animal cell colony into the hollow pin.

Further, the invention is directed to an apparatus for picking animal cell colonies comprising a picking head comprising a plurality of hollow pins connected to a drive that introduces a distal end of the hollow pins into the sample container *offset from the animal cell colony*, such that the animal cell colonies are picked from the medium by the hollow pins at *an offset distance*.

Moreover, the invention is directed to methods of using the apparatus of the invention for identifying and picking animal cell colonies.

The claimed methods and apparatus are specifically designed to pick animal cell colonies without creating any contact between the picking pin and the cell colony, such that animal cell colonies are not destroyed and surrounding cell colonies are not displaced from their position. As discussed during the interview, contact between the picking pin and the animal cell colony disrupts the cell colony and displaces surrounding colonies, and once the animal cell colonies are displaced, the possibility of aspirating the colony is lost.

Furthermore, the claimed invention relies on an integrated imaging system and picking robot to achieve its objects.

## **2. The Cited References Fail to Teach Each and Every Element of the Claimed Invention**

The primary reference, Uber, discloses a system that applies image processing and robotic techniques for automatically picking bacteria or yeast colonies from Petri dishes. Uber fails to disclose or suggest at least three elements of the claimed invention.

First, Uber does not disclose or suggest an apparatus for picking animal cell colonies. Rather, Uber discloses an apparatus for picking *bacteria or yeast colonies*. See Introduction at page 642. The picking of bacterial or yeast colonies is different from the picking of animal cell colonies, because animal cell colonies are greater in size than bacterial or yeast colonies and fewer in number. Thus, the picking mechanism used for bacteria or yeast colonies cannot necessarily be used for animal cell colonies. Second, Uber does not disclose or suggest an integrated imaging and picking robot. Instead, Uber discloses two separate systems: a) an imaging system to digitize and store the image of a dish and establish the coordinates of the colonies in the dish. See Imaging Procedure at page 643 and Figure 2; and b) a Hewlett-Packard Microassay System robot for colony picking. See Robotic System at page 644 and Figure 4. Third, Uber fails to disclose or suggest a non-contact picking apparatus, where the hollow pin is introduced into the medium proximate to the cell colony “by an offset distance.” As discussed above, this “offset distance” allows colonies to be picked without disruption or displacement.

The Office Action recognizes deficiencies in the primary reference. Specifically, the Office Action acknowledges that Uber *does not expressly disclose a plurality of hollow pins connected to the picking head*. See pages 2-3. The Office Action relies on the disclosure of Bienert for the teachings of an automatically controlled metering head comprising a plurality of micropipette tubes for the aspiration of fluids from a sample container and their disposition in a dispensing container. Bienert, however, does not remedy the deficiencies of Uber.

Bienert discloses a metering head for holding, moving and releasing fluid samples. Thus, Bienert fails to disclose or suggest two elements of the claimed invention. First, Bienert does not disclose or suggest a method and an apparatus for picking animal cell colonies. Instead, Bienert discloses an apparatus for picking *fluid samples*. See paragraphs [0002] and [0003] at page 1. Second, Bienert, like Uber, fails to disclose or suggest a non-contact picking apparatus. Thus, Bienert fails to remedy the deficiencies of Uber.

**3. There is no Motivation or Suggestion to Combine the References**

The present obviousness rejection improperly selects isolated teachings from the cited references and combines them in an effort to draw conclusions regarding the claimed invention, when there is no teaching, suggestion or motivation to do so.

For example, the Office Action at page 3 states that it would have been obvious to construct the apparatus of Uber with a picking head comprising a plurality of hollow pins capable of independently collecting cell samples using suction, and subsequently dispensing the samples at a different location. However, there would have been no motivation to combine the two cited references to devise a method and apparatus for picking animal cell colonies, as claimed in the present application, because these references are directed to different fields of endeavor: Uber discloses a method and apparatus for the picking of bacterial or yeast colonies, whereas the invention of Bienert is directed to a system for moving and releasing fluid samples. Because methods and apparatuses for the analysis of fluid samples are very different from those used for the picking of bacterial and yeast colonies, and neither is applicable for picking animal cell colonies, one of skill in the art would simply have no reason to modify the apparatus of Uber by inserting a picking head comprising a plurality of hollow pins, as disclosed by Bienert, to devise the non-contact method and apparatus for picking animal cell colonies claimed in the present application.

**4. One of Skill in the Art Would Have no Expectation of Success**

One of skill in the art would not have a reasonable expectation of success in modifying the references to arrive at the claimed invention for at least two reasons.

First, as stated above, methods and apparatuses for picking bacterial and yeast cell colonies or fluid samples cannot be used for animal cell colonies because of the different size and nature of animal cell colonies. Thus, the artisan skilled in the art would have no reasonable expectation of success in adapting the apparatus of Uber or the apparatus of Bienert for use in picking animal cell colonies.

Second, both Uber and Bienert fail to disclose or suggest a non-contact picking method and apparatus. Thus, the artisan skilled in the art would not expect that introducing a hollow pin of the apparatus into the medium proximate to the animal cell colony by an offset distance would result in an effective aspiration of the animal cell colony into the hollow pin.

For at least these reasons, the rejection of claims 10 and 21 under 35 U.S.C. § 103(a) is improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

**B. Rejection Over Magnuson in view of Elverd**

The Office Action, at pages 3-5, maintains the rejection of claims 1, 3, 10 and 13 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent Application Publication No. 2003/0179916 A1 (“Magnuson”) in view of U.K. Patent Application No. 2310006 A (“Elverd”). Applicants respectfully traverse the rejection.

The Office has failed to establish a *prima facie* case of obviousness, because, as detailed below, none of the criteria necessary to satisfy the burden of factually supporting a *prima facie* conclusion of obviousness under 35 U.S.C. § 103 is satisfied.

**1. The Cited References Fail to Teach Each and Every Element of the Claimed Invention**

The primary reference, Magnuson, discloses a method and apparatus for picking animal cell colonies comprising contacting a picking pin to the base of a sample container and aspirating, or scraping and then aspirating, the cell colonies from the surface of a growth substrate. See paragraphs [0024] at page 3 and [0067] at page 6. Magnuson specifically teaches:

*“a tip is designed with regard to the mechanism by which a colony or cell is to be removed from a growth substrate. For example, if the removal is to be exclusively via aspiration techniques, a tip can be designed such that it can form an essentially airtight seal with the colony or cell, making the removal of the cell or colony more efficient. Alternatively, if the removal is to be via a physical scraping motion, a tip can be*

*designed with a suitable scraping surface adapted to scrape a colony from the growth substrate. If a tip is to operate via a combined aspiration and scraping technique, the tip can be formed with both a scraping edge, which is formed of angles and dimensions that still permit the tip to form a seal with a cell or colony to be isolated.”*

See Paragraph [0127] at page 11 (Emphasis added).

Thus, Magnuson fails to disclose or suggest an essential element of the claimed invention: Magnuson does not disclose or suggest a method and an apparatus for picking animal cell colonies, where the hollow pin is introduced into the medium proximate to the cell colony by an “offset distance,” such that there is *no contact* between the pin and the animal cell colony.

Rather, Magnuson teaches that the contact between the picking pin and the colony is necessary. Thus, Magnuson teaches away from the claimed invention by failing to recognize that contact between the picking pin and the animal cell colony disrupts the cell colony and displaces surrounding colonies.

The Office Action recognizes deficiencies in the primary reference. Specifically, the Office Action acknowledges that Magnuson *does not expressly disclose a plurality of hollow pins used in the collection of animal cells.* See page 4. The Office Action relies on the disclosure of Elverd for the teachings of a picking head comprising a plurality of pins capable of automatically transporting biological cells from a sample container to a dispensing container.

Elverd, however, does not remedy the deficiencies of Magnuson. Elverd discloses a mechanical head comprising a plurality of pins for transferring biological samples. Elverd teaches that “*whenever a piston in the pneumatic actuator is fired it hits a sprung pin in the 96 pin picking head, which is **fired forwards**, enabling it to pick a colony.*” See bottom paragraph at page 2 (Emphasis added). Thus, Elverd, like Magnuson, fails to disclose or suggest a method and an apparatus for picking animal cell colonies, where the hollow pin is

introduced into the medium proximate to the cell colony by **an “offset distance,”** such that there is no contact between the pin and the animal cell colony, as claimed in the present application.

**2. There is no Motivation or Suggestion to Combine the References**

The Office Action at pages 4-5 states that *“it would have been obvious to ensure that the invention disclosed by Magnuson contained a plurality of hollow pins each individually aligned with the characteristic spacing of the wells located in the dispensing container.”* The Office Action further states that *“the use of hollow tubes correlating to multiple wells reduces cross contamination since different tubes are used to collect different samples*

However, this alleged motivation to modify the apparatus disclosed by Magnuson is not found in the prior art. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) holds that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not be based on Applicant’s disclosure. Thus, the rejection is improper and should be withdrawn.

Furthermore, there would have been no motivation to combine the two cited references to devise a method and apparatus for picking animal cell colonies, such that there is no contact between the picking pin and the animal cell colony, because none of the cited references discloses a method and apparatus for picking animal colonies without creating any contact between the picking pin and the colonies. As explained above, both references teach against an apparatus comprising hollow pins that pick animal cell colonies from the medium at an offset distance. One of skill in the art would simply have no reason to modify the apparatus and method disclosed by Magnuson or the apparatus and method disclosed by Elverd to devise the non-contact method and apparatus for picking animal cell colonies claimed in the present application. Thus, the cited references do not support the obviousness rejection.



**3. One of Skill in the Art Would Have no Expectation of Success**

One of skill in the art would not have a reasonable expectation of success in modifying the references to arrive at the claimed invention because, as stated above, the cited references fail to disclose or suggest a non-contact picking method and apparatus. Thus, the artisan skilled in the art would not expect that introducing a hollow pin of the picking apparatus into the medium proximate to the animal cell colony by an offset distance would result in an effective aspiration of the animal cell colony into the hollow pin.

For at least the reasons stated above, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 3, 10 and 13 under 35 U.S.C. § 103(a).

**C. Rejection over Magnuson in view of Elverd  
and further in view of Sogi or Parekh**

The Office Action at pages 6-7 maintains the rejection of claims 4, 11 and 12 under 35 U.S.C. § 103(a) as being unpatentable over Magnuson in view of Elverd and further in view of U.S. Patent No. 4,210,724 (“Sogi”).

Further, at pages 7-10, the Office Action maintains the rejection of claims 4, 7-9, 14-17 and 20 under 35 U.S.C. § 103(a) as being unpatentable over Magnuson in view of Elverd and further in view of U.S. Patent No. 6,064,754 (“Parekh”).

The inability of Magnuson and Elverd to teach or suggest the invention of claims 1, 3, 10 and 13 is demonstrated above. The additional references, Sogi and Parekh, do not remedy the deficiencies of Magnuson and Elverd. Rather, Sogi is directed to an apparatus for liquid disposal and distribution for use in an automatic culture, and Parekh is drawn to computer-assisted methods and apparatus for identifying, selecting and characterizing biomolecules in a biological sample. Both references fail to teach or suggest the non-contact picking method and apparatus claimed in the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 4, 11 and 12 and claims 4, 7-9, 14-17 and 20 under 35 U.S.C. § 103(a).

**CONCLUSION**

All of the stated grounds of rejections have been properly traversed or rendered moot. Therefore, the present application is now in condition for allowance, and an early notice to that effect is earnestly solicited.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date

Nov 9, 2006

By

Michele M. Simkin

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5538  
Facsimile: (202) 672-5399

Michele M. Simkin  
Attorney for Applicants  
Registration No. 34,717